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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.

EXAMINER	
ART UNIT	PAPER NUMBER
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DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/418,176	Applicant(s) Das, G.
	Examiner Peter Tung	Group Art Unit 1652

Responsive to communication(s) filed on _____.

This action is **FINAL**.

Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

X Claim(s) 1-14 is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

Claim(s) _____ is/are allowed.

X Claim(s) 1-4 is/are rejected.

X Claim(s) 5-14 is/are objected to.

Claims _____ are subject to restriction or election requirement.

Application Papers

See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

The drawing(s) filed on _____ is/are objected to by the Examiner.

The proposed drawing correction, filed on _____ is approved disapproved.

The specification is objected to by the Examiner.

The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

X Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

X All Some* None of the CERTIFIED copies of the priority documents have been

received.

X received in Application No. (Series Code/Serial Number) 08/624,398.

received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

X Notice of References Cited, PTO-892

Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

Interview Summary, PTO-413

Notice of Draftsperson's Patent Drawing Review, PTO-948

Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. Claims 1-14 are pending.

Specification

2. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

3. The following title is suggested: "DNA molecules for expression of Bile Salt Stimulaed Lipase."

Claim Objections

4. Claims 5-7, 10 and 14 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from any other multiple dependent claim, either directly or indirectly. Claims 8, 9, 11-13 are objected as they depend upon an improper multiple dependent claim. See MPEP § 608.01(n). Accordingly, the claims have not been further treated on the merits.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112.

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6 Claim 1- 4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7 Claim 1 is indefinite as what "BSSL" represents is not provided in the instant claim.

8 The term "substantially similar" in claim 2 is a relative term which renders the claim indefinite. The term "substantially similar" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The use of "substantially similar" makes the DNA which encodes a peptide other than amino acids -20 to -1 of SEQ ID NO: 2 unclear and ambiguous.

9. The term "biologically active variant" in claims 1 and 4 is a relative term which renders the claim indefinite. The term "biologically active variant" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. All proteins would be considered "biologically active." One of ordinary skill in the art would not know what the metes and bounds are of a variant of BSSL. If a specific activity of human BSSL is being referred to, that activity should be specifically claimed.

10 Claim 4 is unclear if a variant of human BSSL is limited in the instant claim to those human BSSL comprising at least one deletion of the repeat unit consisting of SEQ ID NO: 1.

11. Claim 4 is unclear as the use of "being indicated in" makes the metes and bounds of SEQ ID NO: 1 unclear. Replacing "being indicated in" with "consisting of" would overcome this rejection.

12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The instant claims are directed to DNA encoding a biologically active variant of human BSSL. However, only the DNA sequence encoding human BSSL has been disclosed. Those DNA encoding a biologically active variant of human BSSL have not been disclosed. The specification and claims do not indicate what distinguishing attributes are shared by the members of the claimed genus of DNA encoding a biologically active variant of human BSSL. The scope of the claim includes numerous chemical species with widely differing structural, chemical and physical characteristics and the genus is highly variable because for DNA encoding a biologically active variant of human BSSL, a significant number of structural differences between genus members is permitted. The specification and the claims do not provide any guidance as to what is essential to the operation and function of the claimed DNA encoding a variant BSSL polypeptide and what characteristics could distinguish compounds in the genus of DNA encoding a

biologically active variant of human BSSL from others in the genus are missing from the disclosure. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variable, a single disclosed member of the genus is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus of DNA encoding a biologically active variant of human BSSL. *see University of California v. Eli Lilly and Co.* 43 USPQ2d 1398.

14. Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a DNA molecule comprising a *P. pastoris* methanol oxidase promoter, does not reasonably provide enablement for a DNA molecule comprising a functionally equivalent promoter. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. Factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. The breadth of the instant claims encompass a DNA comprising any functionally equivalent promoter. However, insufficient examples or guidance is provided on what

comprises a functionally equivalent promoter to the methanol oxidase promoter of *P. pastoris*. The skill of those in the art is low in making a functionally equivalent promoters due to the complexities of promoter structure-function relationships. Undue experimentation would be required to determine/make promoters functionally equivalent to the *P. pastoris* methanol oxidase promoter. The scope of the claims is beyond the enabling scope of the disclosure.

Double Patenting

15. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

16. Claims 1-4 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim of U.S. Patent No. 5,827,683 in view of Martinez et al. Claim 1 of U.S. Patent No. 5,827,683 teaches variants of human BSSL where repeat units of BSSL are deleted. U.S. Patent No. 5,827,683 does not teach DNA encoding a human BSSL linked with a S. cerevisiae invertase signal peptide under the control of a methanol oxidase promoter. Martinez et al. teach (page 4, lines 11-17) an expression vector comprising a *P. pastoris* methanol oxidase promoter followed by the DNA sequence encoding the signal peptide

of the sucrose invertase gene of *S. cerevisiae*. Martinez et al. also teach (page 5, line 48 to page 6, line 11) that high level expression and secretion of protein are obtained using this expression vector in *P. pastoris*. Martinez et al. do not teach DNA encoding a variant of human BSSL. It would have been obvious to one of ordinary skill in the art at the time the invention was made to clone the DNA encoding the variant BSSl as taught by U. S. Patent No. 5,827,683 into the *P. pastoris* expression vector taught by Martinez et al. for the benefit of an expression vector which can be used to produce large amounts of secreted BSSL in *P. pastoris*. One of ordinary skill in the art is motivated to combine the two references as Martinez et al. teach a general expression vector for high level production of proteins by secretion. One of ordinary skill in the art would have a reasonable expectation of success at constructing an expression vector according to the teachings of Martinez et al. and containing the DNA encoding the variant human BSSl according to the teachings of U.S Patent No. 5,827,683 as constructing expression vectors containing DNA inserts is well known in the art. Therefore the invention as a whole would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made.

Claim Rejections - 35 USC § 103

17 The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

18 Claims 1, 2 and 4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tang et al. (U.S. Patent No. 5,200,183) in view of Stroman et al. (U.S. Patent No. 4,808,537). Tang et al. teach DNA encoding human bile salt-stimulated lipase and biologically active variants of the enzyme, including variants of the 11- amino acid repeats (column 5, line 61- column 6, line 52 and Figure 2; column 13, lines 9-14, column 14, lines 13-18). Tang et al. teach that the N-terminus of BSSL has exact sequence identity with amino acids -20 to -1 of SEQ ID NO:2. The reference teaches that expression of BSSL can be done, using the appropriate expression vectors, in a yeast host as a cytosolic or secreted protein (column 10, lines 52-64; column 11, lines 21-30). Tang et al. do not teach a *Pichia pastoris* expression vector. Stroman et al. teach *Pichia* expression vectors containing a *Pichia pastoris* alcohol oxidase promoter and the expression of protein in *Pichia pastoris* GS115 using these vectors (column 17, line 59 - column 21, line 18). Stroman et al. do not teach DNA encoding human bile salt-stimulated lipase. It would have been obvious to one of ordinary skill in the art at the time the invention was made to clone DNA encoding human bile salt-stimulated lipase and its variants as taught by Tang et al. into the *Pichia* expression vector taught by Stroman et al. for the benefit of having an expression vector for high level expression of BSSL in *Pichia pastoris*. One of ordinary skill in the art is motivated to combine the two teachings as Tang et al. teach expression of the lipase in yeast and Stroman et al. teach expression vectors for *Pichia pastoris* expression. One of ordinary skill in the art would have a reasonable expectation of success at doing this because the DNA encoding human bile salt-

stimulated lipase as taught by Tang et al. would be expected to be capable of being cloned into, according to the teachings of Stroman et al., a *Pichia* expression vector. Therefore the invention as a whole would have been prima facie obvious to one of ordinary skill at the time the invention was made.

19. Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Tang et al. (U.S. Patent No. 5,200,183) in view of Martinez et al. Tang et al. teach DNA encoding human bile salt-stimulated lipase and biologically active variants of the enzyme (column 5, line 61- column 6, line 52 and Figure 2, column 13, lines 9-14, column 14, lines 13-18). Tang et al. teach that human milk BSSL has a 20 amino acid signal sequence and that the mature lipase comprises the 722 remaining amino acids(column 2, lines 13-15). The reference teaches that expression of BSSL can be done, using the appropriate expression vectors, in a yeast host as a cytosolic or secreted protein (column 10, lines 52-64; column 11, lines 21-30). Tang et al. do not teach a *Pichia pastoris* expression vector. Martinez et al. teach an expression vector comprising a *Pichia pastoris* alcohol oxidase promoter followed by the signal peptide of the sucrose invertase gene of *Saccharomyces cerevisiae* (page 4, lines 11-17). Martinez et al. teach the high level expression and secretion of protein when using this expression vector in transformed *Pichia pastoris* (page 5, line 48- page 6, line 11). It would have been obvious to one of ordinary skill in the art at the time the invention was made to clone the DNA encoding mature lipase (BSSL) and its variants as taught by Tang et al. into the *Pichia pastoris* expression vector taught by Martinez et al. for the benefit of having an expression vector for high level secretion expression of BSSL in *Pichia*

pastoris. One of ordinary skill in the art is motivated to combine the two teachings as Tang et al. teach expression of the lipase in yeast and Martinez et al. teach expression vectors for *Pichia pastoris* expression. One of ordinary skill in the art would have a reasonable expectation of success at doing this because it is a reasonable expectation to be able to clone the DNA encoding mature BSSL and its variants as taught by Tang et al. into the *Pichia pastoris* expression vector comprising DNA encoding a sucrose invertase signal peptide, as taught by Martinez et al., as making such expression vector constructs are well known in the art. Therefore the invention as a whole would have been prima facie obvious to one of ordinary skill at the time the invention was made.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Peter Tung, Ph.D. whose telephone number is (703) 308-9436. The examiner can normally be reached on Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy, Ph.D., can be reached on (703) 308-3804. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

PONNATHAPU ACHUTAMURTHY
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600